CLAIMS

1. A monomeric, cyclic peptide analogue of a B-chain of a relaxin superfamily member protein which binds to a biological target of the relaxin superfamily protein, and modulates an activity of the biological target, wherein the relaxin superfamily protein is selected from insulin, IGF-I, IGF-II, relaxin 1, relaxin 2, relaxin 3, INSL3, INSL4, INSL5 and INSL6, the biological target being selected from insulin receptors, IGFR-I, IGFR-II, LGR7 and LGR8.

2. The analogue according to claim 1, wherein the analogue is produced by modification of a turn or loop moiety of the B-chain of the relaxin superfamily protein, the modification involving selection of at least a first and a second amino acid residue with an alpha-helix or beta-strand carbon separation distance of less than six angstroms and cross-linking the first and second amino acids, wherein the cross-link conformationally constrains the analogue.

3. The analogue according to claim 1 or claim 2, wherein the analogue is an INSL3 B-chain analogue modified from a sequence set forth in SEQ ID NO:7.

4. The analogue according to claim 3, wherein the INSL3 analogue is constrained by a cross-link between a first amino acid within a range of positions 2 and 8 and a second amino acid within a range of positions 21 and 26 of the sequences set forth in SEQ ID NO:7.

5. The analogue according to any one claims 3 to 4, wherein the analogue is the INSL3 analogue designated cINSLa in Figure 3.

6. The analogue according to any one of claims 3 to 4, wherein the analogue is the INSL3 analogue designated cINSLb in Figure 3.

7. The analogue according to claim 1 or claim 2, which is a relaxin analogue modified from a relaxin-1, relaxin-2, or relaxin-3 B-chain sequence set forth in SEQ ID NOs:1, 2 and 3, respectively.

8. The analogue according to claim 7, wherein the relaxin analogue is constrained by a cross-link between a first amino acid within a range of positions 2 and 8 and a second amino acid within a range of positions 21 and 26 of the sequences set forth in SEQ ID NO:2.

9. The analogue according to claim 8, wherein the relaxin analogue is the relaxin analogue designated cRlx in Figure 3.

10. The analogue according to any one of claims 2, wherein the first and/or second amino acids are substituted with alternative amino acids suitable for cross-linking.

11. The analogue according to 10 wherein at least one of the alternative amino acids is a cysteine residue.

12. The analogue according to 11 wherein both of the alternative amino acid residues are cysteine residues.

13. The analogue according to 12 wherein the analogue is cross-linked by oxidizing the cysteine residues to form a disulfide bond between the cysteine residues.

14. An analogue according to any one of claims 1 to 13, wherein one or more amino acids within the INSL3 or relaxin peptide analogue sequence, other than the cross-linked first and second amino acids, is optionally substituted to modify one or more biological activities of the analogue.

15. The analogue according to any one of claims 1 to 14 wherein the biological target of the analogue is LGR7 and/or LGR8.

16. The analogue according to claim 15, wherein activity of the biological target is initiated, up-regulated, down-regulated or otherwise blocked.

17. The analogue of any of the preceding claims, wherein the analogue is conjugated to an A-chain of a relaxin superfamily protein.

18. The analogue according to claim 17, wherein the A-chain of the relaxin superfamily protein is a corresponding A-chain for the relaxin superfamily protein.

19. The analogue according to any one of claims 1 to 18, wherein the analogue is conjugated to a reporter group.

20. The analogue according the claim 19, wherein the reporter group is a radiolabel.

21. The analogue according to claim 19, wherein the reporter group is a fluorescent label.

22, The analogue according to claim 19, wherein the reporter group is an enzyme.

23. The analogue according to claim 19, wherein the reporter group is a carrier.

24. A method of making a peptide analogue of a relaxin superfamily protein, the method comprising:

- providing a B-chain, receptor-binding subunit of a relaxin superfamily protein; and
- identifying a first and a second amino acid on respective, opposing strands of a turn and/or loop moiety in the receptor-binding subunit of the protein, with an alpha-helix or beta-strand carbon separation distance of less than six angstroms; and
- introducing a cross-link between the first and second amino acids;

wherein the cross-link conformationally constrains a three dimensional structure of at the B-chain, receptor-binding subunit.

25. The method according to claim 24, wherein the first and/or second amino acids are substituted with amino acids suitable for cross-linking.

26. The method according to claim 24 or 25, wherein the method produces an INSL3 peptide analogue based on the sequence set forth in SEQ ID NO:7, with the first amino acid within a range of residues 2 and 8 and the second amino acid within a range of residues 21 and 26.

27. The method according to claim 26, wherein the INSL3 analogue is cINSLa as designated in Figure 3.

28. The method according to claim 26, wherein the INSL3 analogue is cINSLb as designated in Figure 3.

29. The method according to claim 24 or 25, wherein the method produces a relaxin-2 peptide analogue based on any of the sequences set forth in SEQ ID NOs:2, with the first amino acid within a range of residues 2 and 8 and the second amino acid within a range of residues 21 and 26..

30. The method according to claim 29, wherein the method produces the relaxin analogue designated cRlx in Figure 3.

31. The method according to any one of claims 24 to 26 or 29, wherein the method produces an INSL3 or relaxin analogue wherein one or more amino acids other than the cross-linked first and second amino acids, are optionally substituted to modify one or more biological activities of the peptide analogue.

32. A pharmaceutical composition including one or more of the analogues as defined in any one of claims 1 to 23, or pharmaceutically acceptable salts thereof.

33. The pharmaceutical compositions according to claim 32, further comprising at least one pharmaceutically acceptable carrier or diluent.

34. A method of treating, preventing or ameliorating the symptoms of a disorder in a patient, the disorder involving disregulation of activity of a relaxin superfamily protein member, the method comprising administering to the patient an effective amount of a peptide analogue according to any one of claims 1 to 23.

35. The method according to claim 34, wherein the disorder is mediated by relaxin or INSL3.

36. The method according to claim 35, wherein the disorder selected from the group consisting of hyperplastic disorders, scleroderma, uncontrolled or abnormal collagen or fibronectin formation or breakdown, neoplastic disorders, neurological disorders, angiogenic disorders, cardiovascular disorders, female reproductive disorders, conditions associated with pregnancy, renal disease, inflammatory bowel disease, Raynaud's disease, Raynaud's phenomenon, cryptorchidism, male or female infertility, disregulation of spermatogenesis and reproductive development including descent of the gonads, the method comprising administering to the patient an effective amount of a peptide analogue according to any one of claims 1 to 23, or a pharmaceutical composition according to any one of claims 32 to 33.

37. The method according to claim 36, wherein the disorder is a female reproductive disorder.

38. The method according to claim 36, wherein the disorder is a pregnancy-related disorder.

39. The method according to claim 36, wherein the disorder involves abnormal reproductive development.

40. The method according to claim 36, wherein the disorder is a cardiovascular disorder.

41. The method according to claim 36, wherein the disorder is an angiogenic disorder.

42. The method according to claim 36, wherein the disorder is a neoplastic disorder or a hyperplastic disorder.

43. The method according to claim 42, wherein the neoplastic or hyperplastic disorder involves the thyroid gland.

44. The method according to claim 36, wherein the disorder is scleroderma.

45. The method according to claim 36, wherein the disorder is renal disease.

46. The method according to claim 36, wherein the disorder involves uncontrolled or abnormal collagen or fibronectin formation or breakdown.

47. The method according to claim 36, wherein the disorder is male or female infertility.

48. Use of the analogues and/or pharmaceutical compositions of the present invention in the manufacture of a medicament for the treatment of a relaxin or INSL3-mediated disorder in a patient.

49. Use according to claim 48, wherein the disorder is selected from the group consisting of: hyperplastic disorders, neoplastic disorders, scleroderma, uncontrolled or abnormal collagen or fibronectin formation or breakdown, neurological disorders, angiogenic disorders, cardiovascular disorders, female reproductive disorders, conditions associated with pregnancy, renal disease, inflammatory bowel disease, Raynaud's disease, Raynaud's

phenomenon, cryptorchidism, disregulation of spermatogenesis and reproductive development including descent of the gonads.